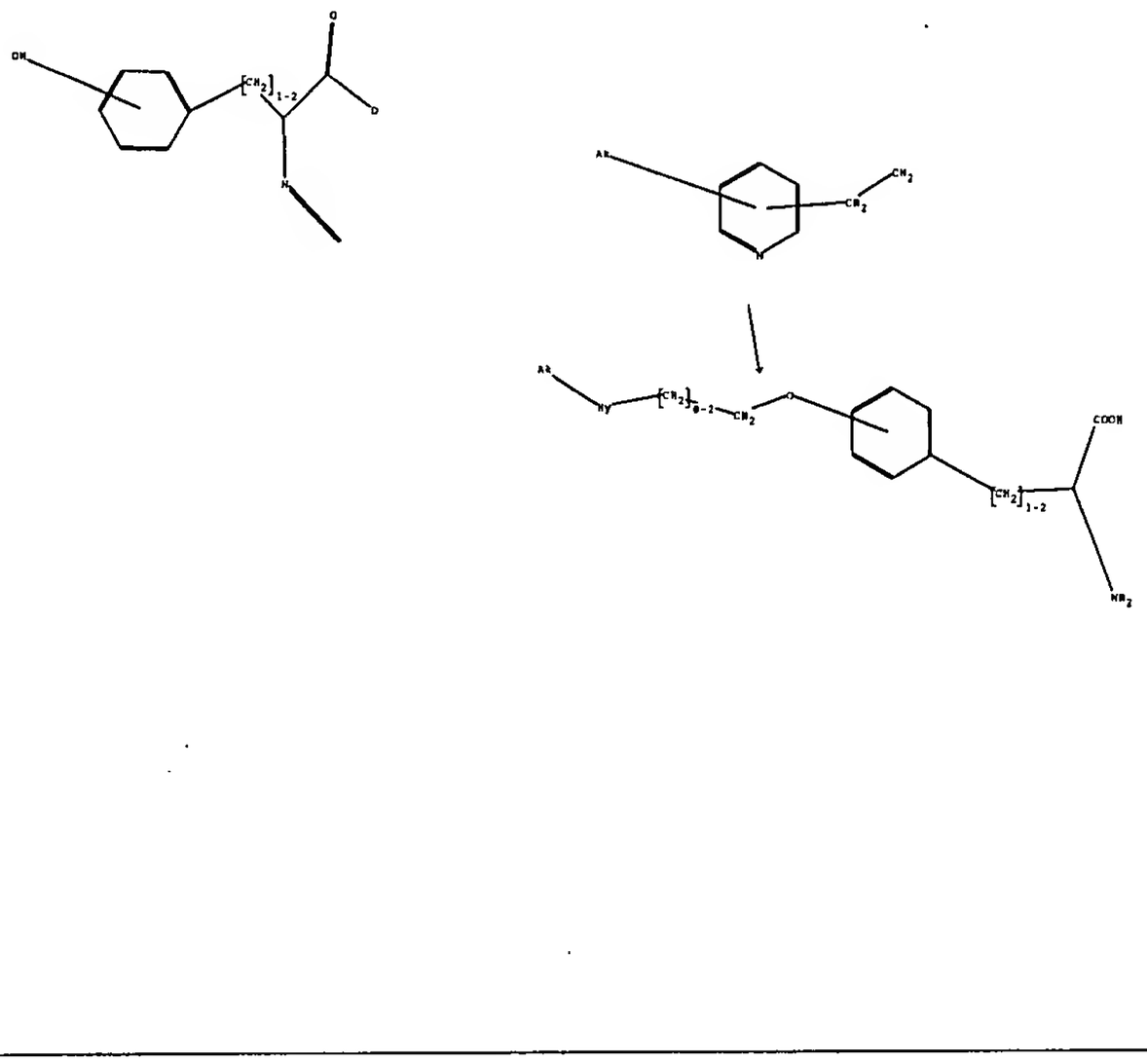
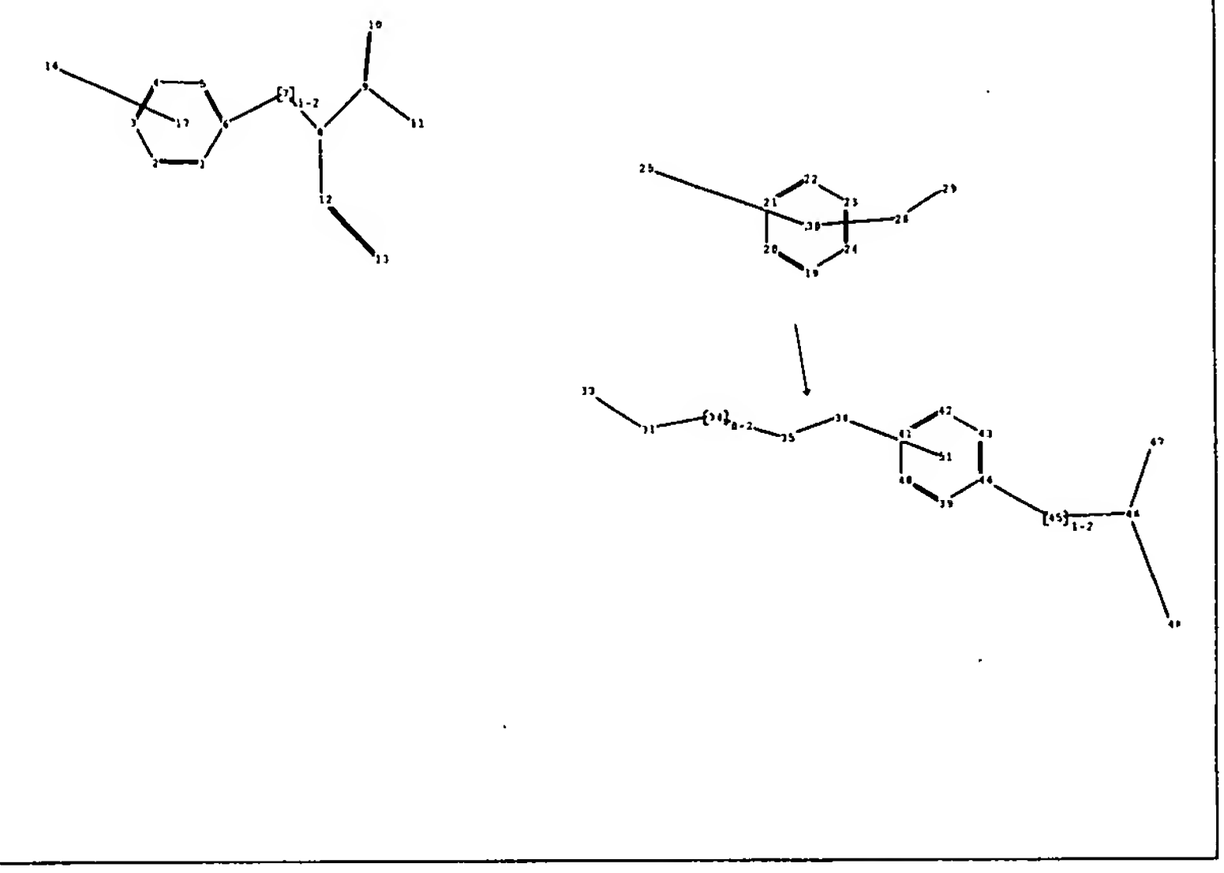
C:\Documents and Settings\brobinson1\My Documents\stnweb\Queries\erereilk.str





chain nodes :
7 8 9 10 11 12 13 16 25 28 29 31 33 34 35 38 45 46 47 48
ring nodes :
1 2 3 4 5 6 19 20 21 22 23 24 39 40 41 42 43 44
chain bonds :
6-7 7-8 8-9 8-12 9-10 9-11 12-13 28-29 31-33 31-34 34-35 35-38
44-45 45-46 46-47 46-48
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 19-20 19-24 20-21 21-22 22-23 23-24
39-40 39-44 40-41 41-42 42-43 43-44
exact/norm bonds :
8-12 9-10 9-11 12-13 31-33 31-34 46-48
exact bonds :
6-7 7-8 8-9 28-29 34-35 35-38 44-45 45-46 46-47
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 19-20 19-24 20-21 21-22 22-23 23-24
39-40 39-44 40-41 41-42 42-43 43-44
isolated ring systems :
containing 1 : 19 : 39 :

Connectivity :
25:1 E exact RC ring/chain 33:1 E exact RC ring/chain
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS
10:CLASS 11:CLASS 12:CLASS 13:CLASS 16:CLASS 17:Atom 19:Atom 20:Atom
21:Atom 22:Atom 23:Atom 24:Atom 25:CLASS 27:Atom 28:CLASS 29:CLASS
30:Atom 31:Atom 33:CLASS 34:CLASS 35:CLASS 38:CLASS 39:Atom 40:Atom
41:Atom 42:Atom 43:Atom 44:Atom 45:CLASS 46:CLASS 47:CLASS 48:CLASS
51:Atom
Generic attributes :
31:
Saturation : Unsaturated
Number of Carbon Atoms : less than 7

```
    Number of Hetero Atoms : Exactly 1
    Type of Ring System    : Monocyclic

fragments assigned reactant role:
    containing 1
    containing 19
fragments assigned product role:
    containing 31
Element Count :
    Node 31: Limited
        C,C5
        N,N1
```

10555659

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1612bxr

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS	4	DEC 18	CA/CAplus patent kind codes updated
NEWS	5	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS	6	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS	7	DEC 27	CA/CAplus enhanced with more pre-1907 records
NEWS	8	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS	9	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS	10	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS	11	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS	12	JAN 22	CA/CAplus updated with revised CAS roles
NEWS	13	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS	14	JAN 29	PHAR reloaded with new search and display fields
NEWS	15	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS	16	FEB 15	PATDPASPC enhanced with Drug Approval numbers
NEWS	17	FEB 15	RUSSIAPAT enhanced with pre-1994 records
NEWS	18	FEB 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS	19	FEB 26	MEDLINE reloaded with enhancements
NEWS	20	FEB 26	EMBASE enhanced with Clinical Trial Number field
NEWS	21	FEB 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS	22	FEB 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS	23	FEB 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
NEWS	24	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS	25	MAR 16	CASREACT coverage extended
NEWS	26	MAR 20	MARPAT now updated daily
NEWS	27	MAR 22	LWPI reloaded
NEWS	28	MAR 30	RDISCLOSURE reloaded with enhancements
NEWS	29	MAR 30	INPADOCDB will replace INPADOC on STN
NEWS	30	APR 02	JICST-EPLUS removed from database clusters and STN

NEWS EXPRESS	NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

Updated Search

10555659

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 12:51:47 ON 11 APR 2007

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 12:51:56 ON 11 APR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 10 APR 2007 HIGHEST RN 929680-66-0
DICTIONARY FILE UPDATES: 10 APR 2007 HIGHEST RN 929680-66-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> file casreact

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.45	0.66

FILE 'CASREACT' ENTERED AT 12:52:00 ON 11 APR 2007
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications.

FILE CONTENT:1840 - 7 Apr 2007 VOL 146 ISS 16

Updated Search

10555659

New CAS Information Use Policies, enter HELP USAGETERMS for details.

```
**************************************************
*                                                *
*     CASREACT now has more than 12 million reactions       *
*                                                *
**************************************************
```

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=>
Uploading C:\Documents and Settings\brobinson1\My
Documents\stnweb\Queries\erereilk.str

L1      STRUCTURE UPLOADED

=>  s l1
SAMPLE SEARCH INITIATED 12:59:48 FILE 'CASREACT'
SCREENING COMPLETE -      452 REACTIONS TO VERIFY FROM       18 DOCUMENTS

100.0% DONE     452 VERIFIED       0 HIT RXNS                    0 DOCS
SEARCH TIME: 00.00.02

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED VERIFICATIONS:      7765 TO    10315
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1 (     0 REACTIONS)

=> s l1 full
THE ESTIMATED SEARCH COST FOR FILE 'CASREACT' IS 113.10 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 12:59:54 FILE 'CASREACT'
SCREENING COMPLETE -     7232 REACTIONS TO VERIFY FROM      550 DOCUMENTS

100.0% DONE    7232 VERIFIED      12 HIT RXNS                   1 DOCS
SEARCH TIME: 00.00.04

L3            1 SEA SSS FUL L1 (    12 REACTIONS)

=> d l3, all, crxn, 1
'CRXN' IS NOT A VALID FORMAT FOR FILE 'CASREACT'

The following are valid formats:

ABS -------- GI and AB
ALL -------- BIB, AB, IND, RE, Single-step Reactions
APPS ------- AI, PRAI
BIB -------- AN, plus Bibliographic Data
CAN -------- List of CA abstract numbers without answer numbers
CBIB ------- AN, plus Compressed Bibliographic Data
DALL ------- ALL, delimited (end of each field identified)
```

Updated Search

10555659

IABS ------- ABS, indented with text labels
IALL ------- ALL, indented with text labels
IBIB ------- BIB, indented with text labels
IND -------- Indexing data
IPC -------- International Patent Classifications
ISTD ------- STD, indented with text labels
OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

MAX -------- Same as ALL
PATS ------- PI, SO
SCAN ------- TI and FCRD (random display, no answer number. SCAN must be entered on the same line as DISPLAY, e.g., D SCAN.)
SSRX ------- Single-Step Reactions (Map, Diagram, and Summary for all single-step reactions)
STD -------- BIB, IPC, and NCL

CRD -------- Compact Display of All Hit Reactions
CRDREF ----- Compact Reaction Display and SO, PY for Reference
FHIT ------- Reaction Map, Diagram, and Summary for first hit reaction
FHITCBIB --- FHIT, AN plus CBIB
FCRD ------- First hit in Compact Reaction Display (CRD) format
FCRDREF ---- First hit in Compact Reaction Display (CRD) format with CA reference information (SO, PY). (Default)
FPATH ------ PATH, plus Reaction Summary for the "long path"
FSPATH ----- SPATH, plus Reaction Summary for the "short path"
HIT -------- Reaction Map, Reaction Diagram, and Reaction Summary for all hit reactions and fields containing hit terms
OCC -------- All hit fields and the number of occurrences of the hit terms in each field. Includes total number of HIT, PATH, SPATH reactions. Labels reactions that have incomplete verifications.
PATH ------- Reaction Map and Reaction Diagram for the "long path". Displays all hit reactions, except those whose steps are totally included within another hit reaction which is displayed
RX --------- Hit Reactions (Map, Diagram, Summary for all hit reactions)
RXG -------- Hit Reaction Graphics (Map and Diagram for all hit reactions)
RXL -------- Hit Reaction Long (Map, Diagram, Summary for all hit reactions)
RXS -------- Hit Reaction Summariers (Map and Summary for all hit reactions)
SPATH ------ Reaction Map and Reaction Diagram for the "short path". Displays all single step reactions which contain a hit substance. Also displays those multistep reactions that have a hit substance in both the first and last steps of the reaction, except for those hit reactions whose steps are totally included within another hit reaction which is displayed

To display a particular field or fields, enter the display field codes. For a list of the display field codes, enter HELP DFIELDS at an arrow prompt (=>). Examples of combinations include: D TI; D BIB RX; D TI, AU, FCRD. The information is displayed in the same order as the specification. All of the formats, except CRD, CRDREF, FHIT, PATH,

Updated Search

FPATH, SPATH, FSPATH, FCRD, FCRDREF, HIT, RX, RXG, RXS, SCAN, and OCC, may be used with the DISPLAY command to display the record for a specified Accession Number.

ENTER DISPLAY FORMAT (FCRDREF):end

=> d his

(FILE 'HOME' ENTERED AT 12:51:47 ON 11 APR 2007)

FILE 'REGISTRY' ENTERED AT 12:51:56 ON 11 APR 2007

FILE 'CASREACT' ENTERED AT 12:52:00 ON 11 APR 2007
L1 STRUCTURE UPLOADED
L2 0 S L1
L3 1 S L1 FULL

=> d l3, ibib abs crd, 1

L3 ANSWER 1 OF 1 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 141:424428 CASREACT
TITLE: Intermediate compound, namely O-[2-(5-ethylpyridin-2-yl)ethyl]tyrosine, which is used for the preparation of the antidiabetic agent pioglitazone, and methods for its preparation and conversion to pioglitazone
INVENTOR(S): Duran, Lopez Ernesto
PATENT ASSIGNEE(S): Medichem, S.A., Spain
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004099147	A1	20041118	WO 2004-ES70031	20040504
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
ES 2219180	A1	20041116	ES 2003-1075	20030509
ES 2219180	B1	20060301		
CA 2525190	A1	20041118	CA 2004-2525190	20040504
EP 1623977	A1	20060208	EP 2004-731028	20040504
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.: ES 2003-1075 20030509
WO 2004-ES70031 20040504

OTHER SOURCE(S): MARPAT 141:424428
GI

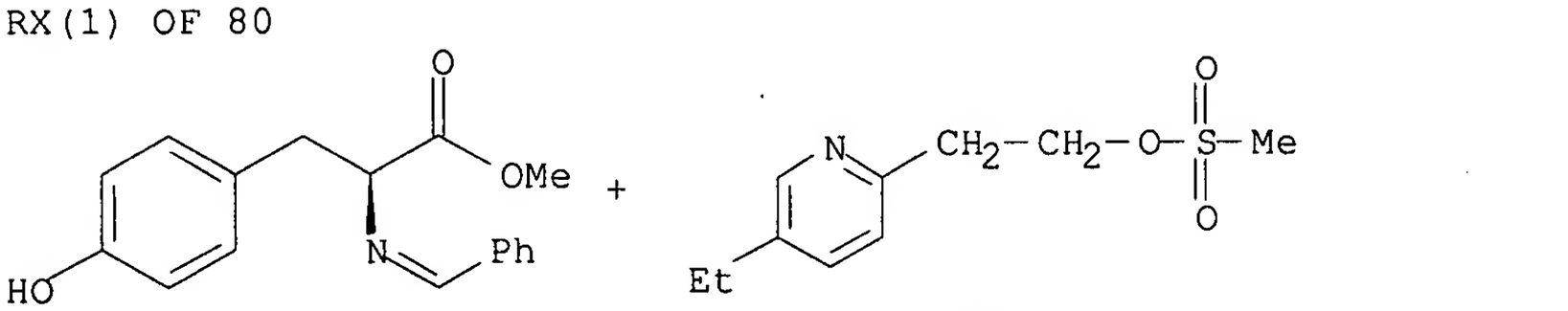
Updated Search

10555659

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

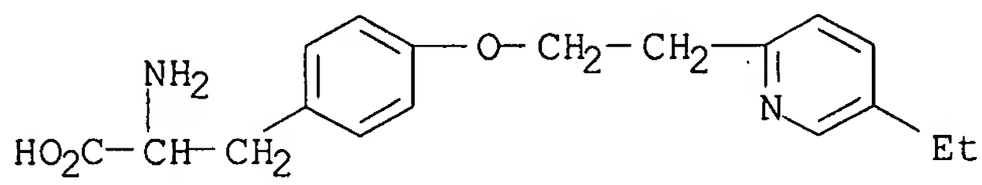
AB The invention relates to the novel O-substituted tyrosine derivative I, including pure or mixed enantiomers, racemates, salts, solvates, and hydrates. I and its stereoisomers and compds. are new key intermediates for the preparation of the antidiabetic agent pioglitazone (II). The invention also relates to a method of obtaining I from a natural product, L-tyrosine, in which the amino group, in the form of an aromatic imine group, is protected by an aldehyde or ketone. The invention further relates to a method of obtaining II from the intermediate compound I. The critical feature of the invention is protection of the tyrosine N-terminal as an imine, which allows etherification of the phenolic tyrosine OH group to occur without competing N-alkylation. Complete racemization during the process allows the more desirable racemic I to be prepared from the more readily available L-tyrosine. For instance, L-tyrosine was treated with SOCl2 in refluxing MeOH to give the Me ester, which was treated with PhCHO at room temperature in CH2Cl2 to give doubly protected tyrosine III. This phenolic compound was etherified with the mesylate IV (preparation given) using K2CO3 and Bu4N+Br- in PhMe at 70°, and the protected product was deprotected in situ first with acid (2N HCl) and then with base (50% NaOH), both at 70°, to give racemic I in 62.8% overall yield from L-tyrosine. Diazotization of the amino group in I in the presence of HBr gave the corresponding bromo compound, which was cyclized with thiourea to give the 2-imine derivative of II. Acid hydrolysis of the imine in refluxing aqueous HCl gave II in 40.7% yield from I. Four comparative processes for preparing I, using other standard amine protecting groups instead of a benzaldehyde imine, were examined Overall yields of I from L-tyrosine were 24.1% for Boc, 20.7% for Cbz, 11.5% for Ac, and poor (unisolated) for EtOCO, vs. 62.8% for benzylidene.

RX(1) OF 80



(step 3) (step 1)

1. PhMe
2. Bu4N.Br, K2CO3
4. PhMe
5. K2CO3
6. Bu4N.Br
7. HCl, Water
8. NaOH, Water
9. HCl, Water

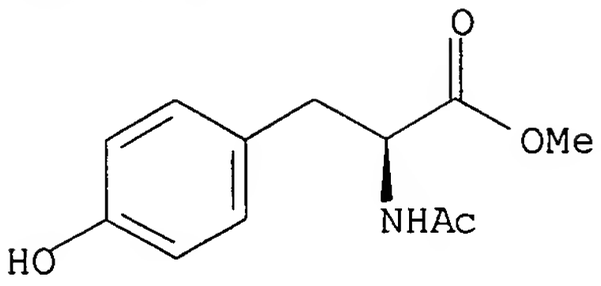


NOTE: last stage neutralization

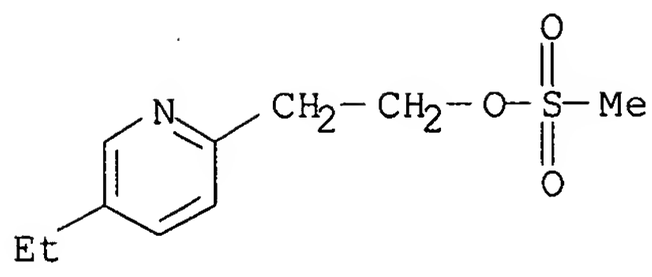
Updated Search

10555659

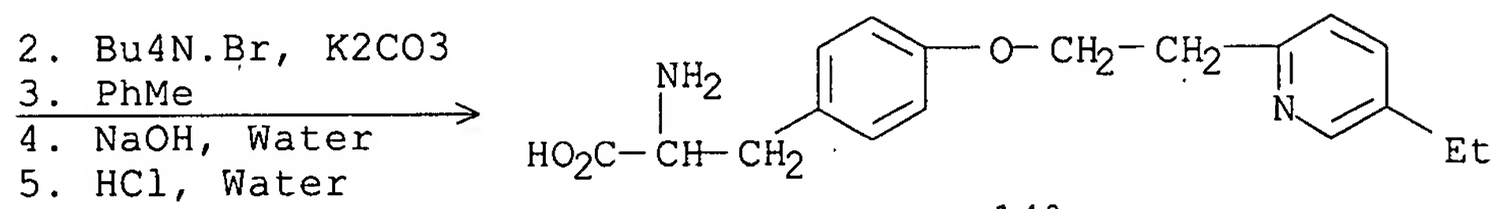
RX(14) OF 80



(step 1)



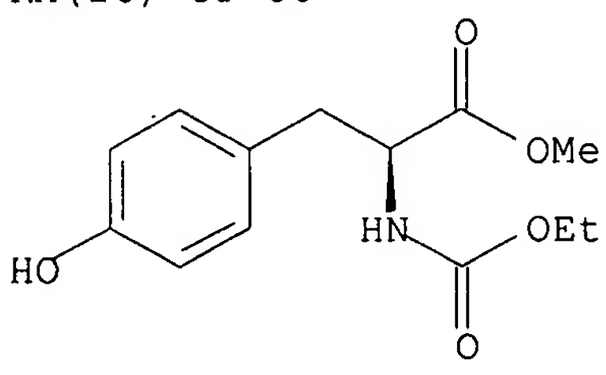
(step 1)



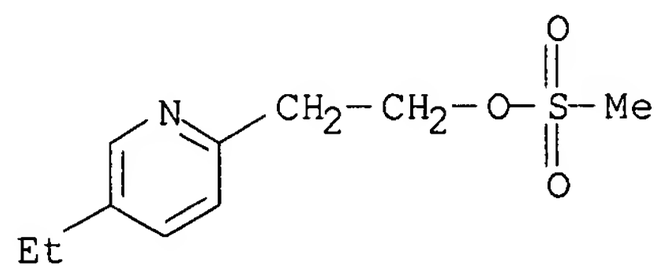
14%

NOTE: last stage neutralization

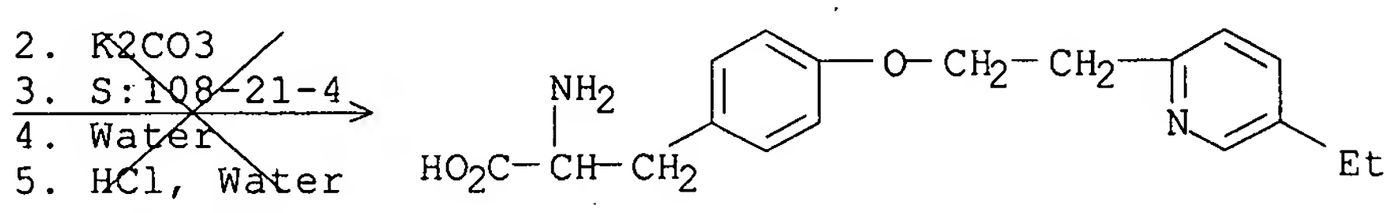
RX(16) OF 80



(step 1)



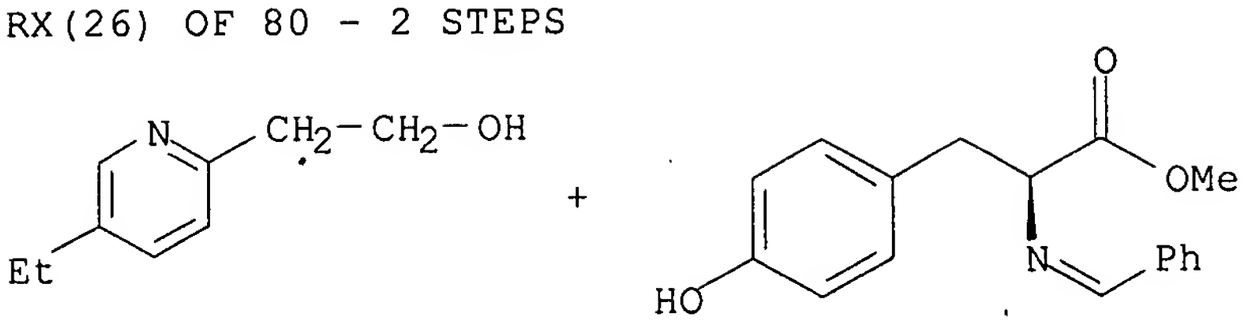
(step 1)



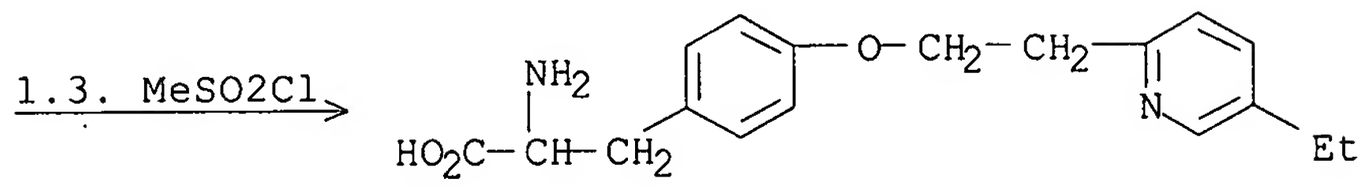
NOTE: failed reaction

Updated Search

RX(26) OF 80 - 2 STEPS

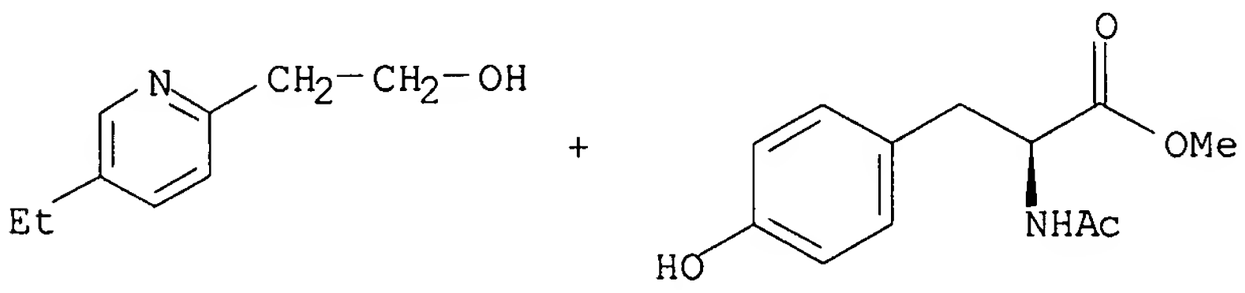


(step 2.3)

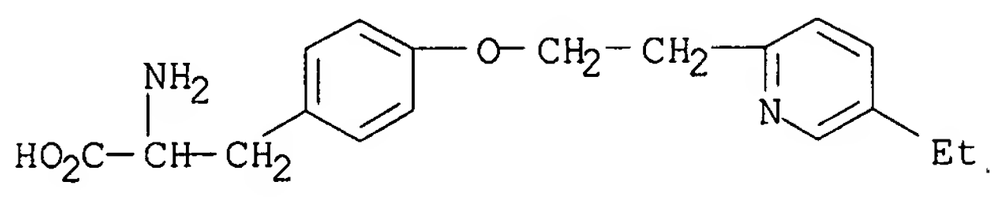


NOTE: 2) last stage neutralization
CON: STEP(1.1) room temperature
STEP(1.2) room temperature -> 0 deg C
STEP(1.3) 75 minutes, 0 - 10 deg C; 10 deg C -> room temperature;
1 hour, room temperature

RX(29) OF 80 - 2 STEPS



1.1. PhMe
1.2. Et3N
1.3. MeSO2Cl
2.2. Bu4N.Br, K2CO3
2.3. PhMe
2.4. NaOH, Water
2.5. HCl, Water

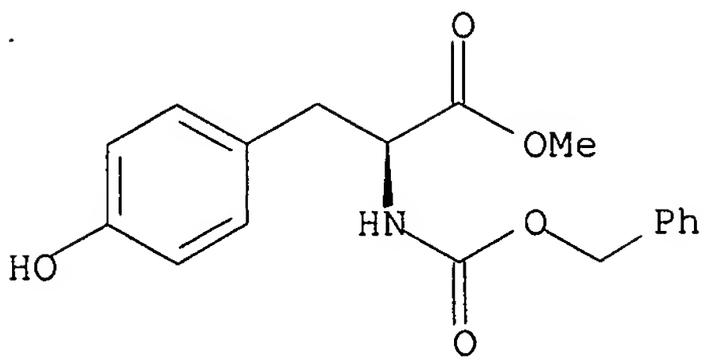


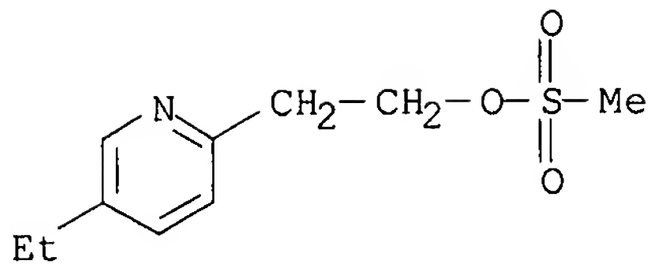
14%

NOTE: 2) last stage neutralization
CON: STEP(1.1) room temperature
STEP(1.2) room temperature -> 0 deg C
STEP(1.3) 75 minutes, 0 - 10 deg C; 10 deg C -> room temperature;
1 hour, room temperature

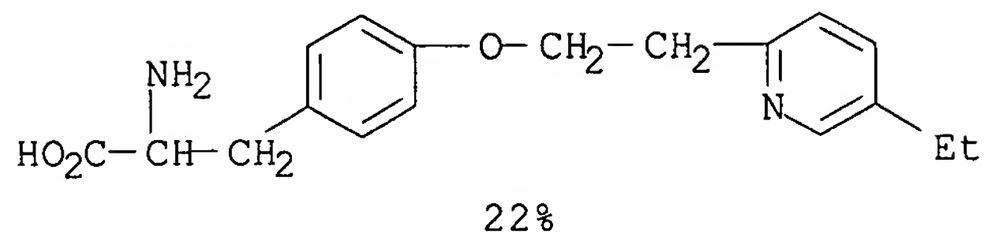
Updated Search

RX(34) OF 80 - 2 STEPS





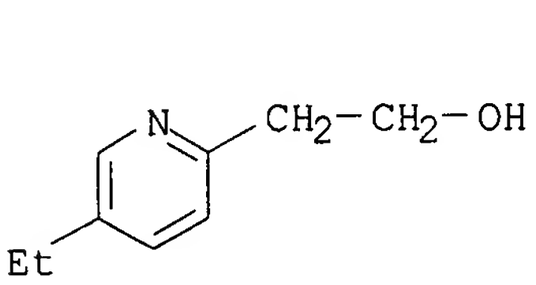
1.1. PhMe
1.2. K2CO3
1.3. S:108-21-4
1.4. Bu4N.Br
2.1. MeOH
2.2. NaOH, Water
2.3. HCl, Water
2.4. NaOH, Water

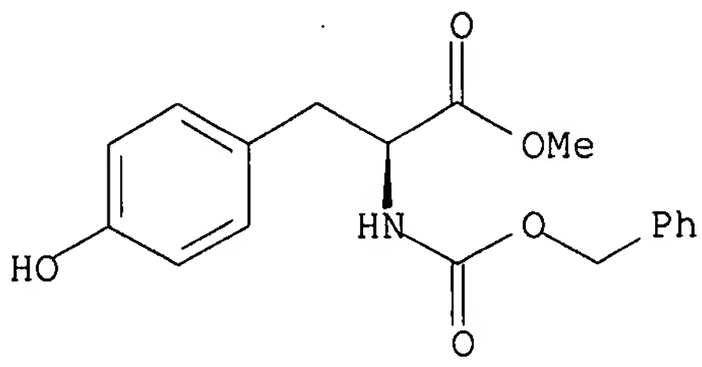


22%

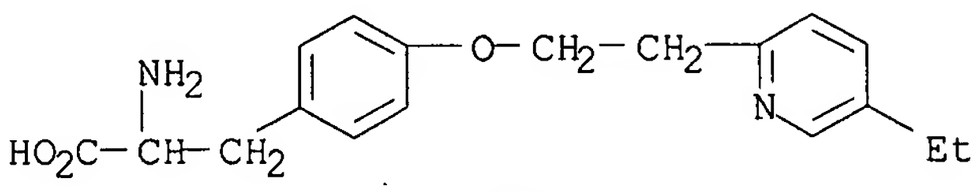
NOTE: 2) last stage neutralization

RX(48) OF 80 - 3 STEPS





1.3. MeSO2Cl



22%

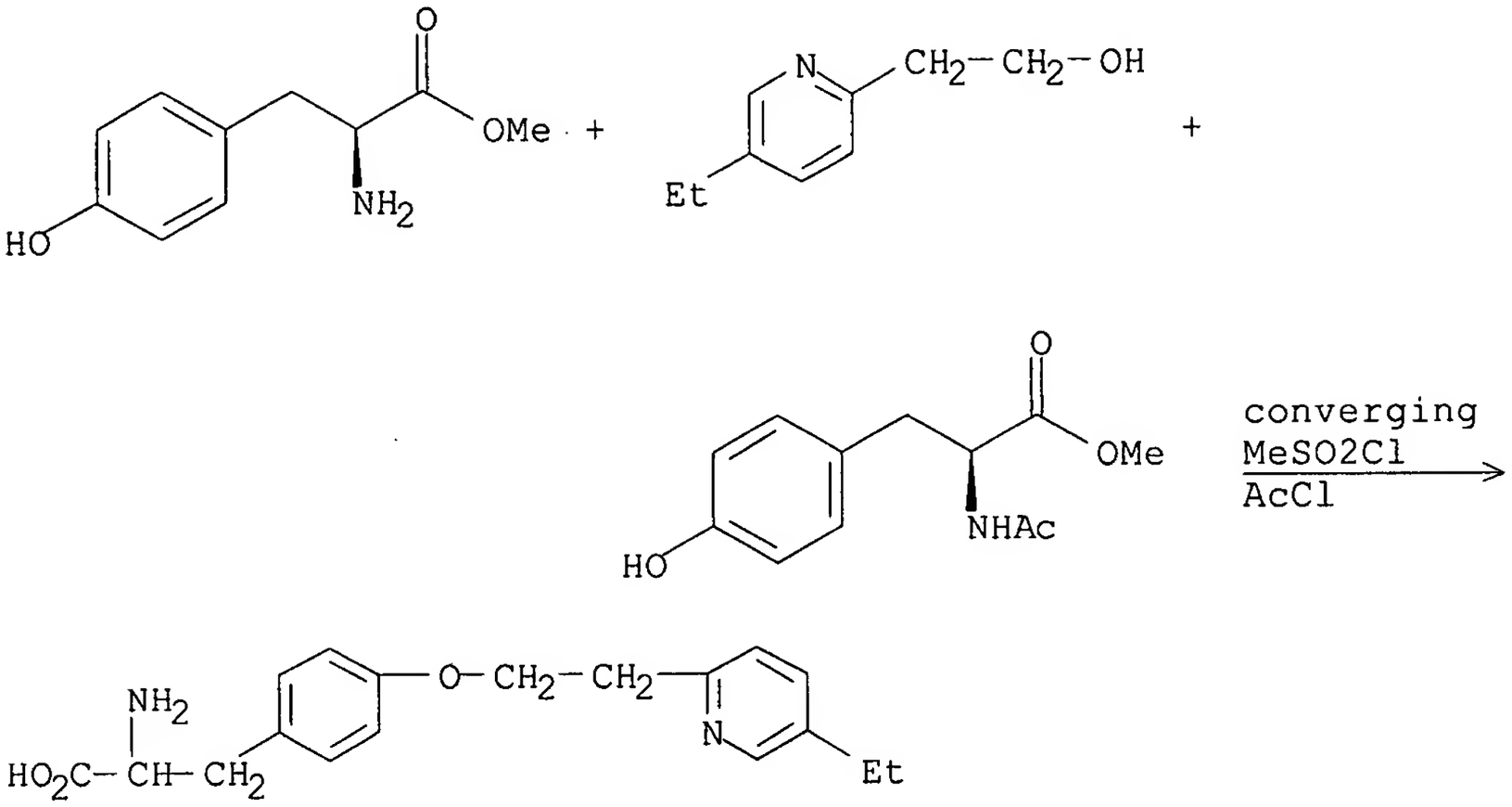
NOTE: 3) last stage neutralization

CON: STEP(1.1) room temperature
STEP(1.2) room temperature -> 0 deg C
STEP(1.3) 75 minutes, 0 - 10 deg C; 10 deg C -> room temperature;
1 hour, room temperature

Updated Search

10555659

RX(49) OF 80 - 3 STEPS

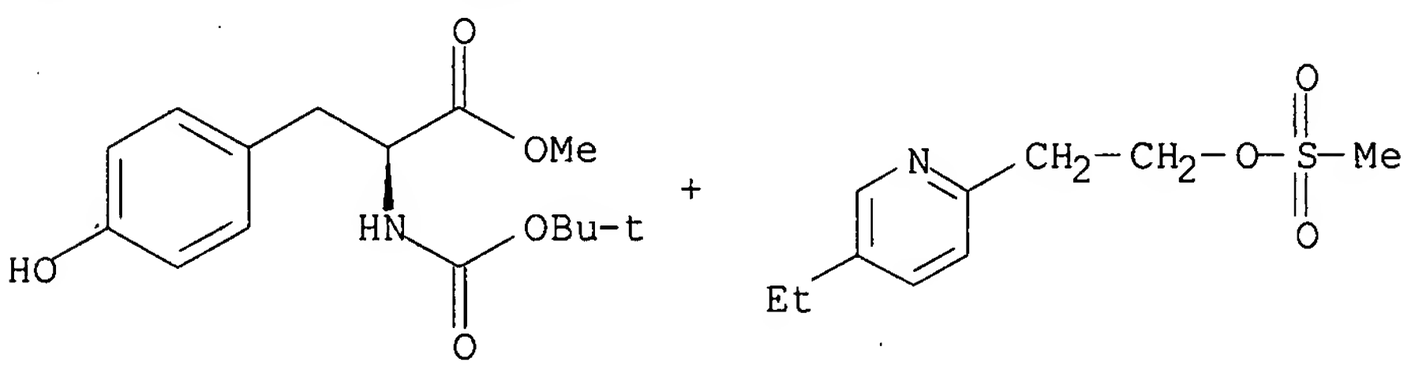


converging
MeSO2Cl
AcCl

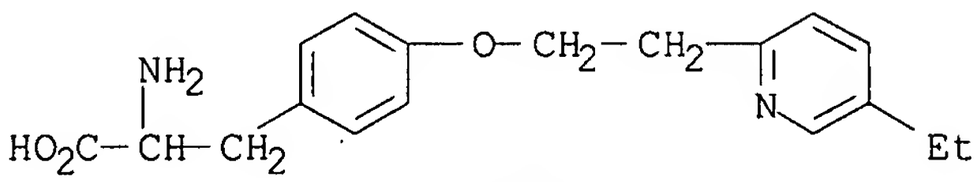
14%

NOTE: last stage neutralization
CON: STEP(1.1) room temperature
STEP(1.2) room temperature -> 0 deg C
STEP(1.3) 75 minutes, 0 - 10 deg C; 10 deg C -> room temperature;
1 hour, room temperature

RX(53) OF 80 - 3 STEPS



1.1. PhMe
1.2. K2CO3
1.3. MeOH, PhMe
2.2. KOH, Water
2.3. MeOH
2.4. SOCl2
2.5. NaHCO3, Water
3.1. Water, MeOH
3.2. KOH
3.3. HCl, Water

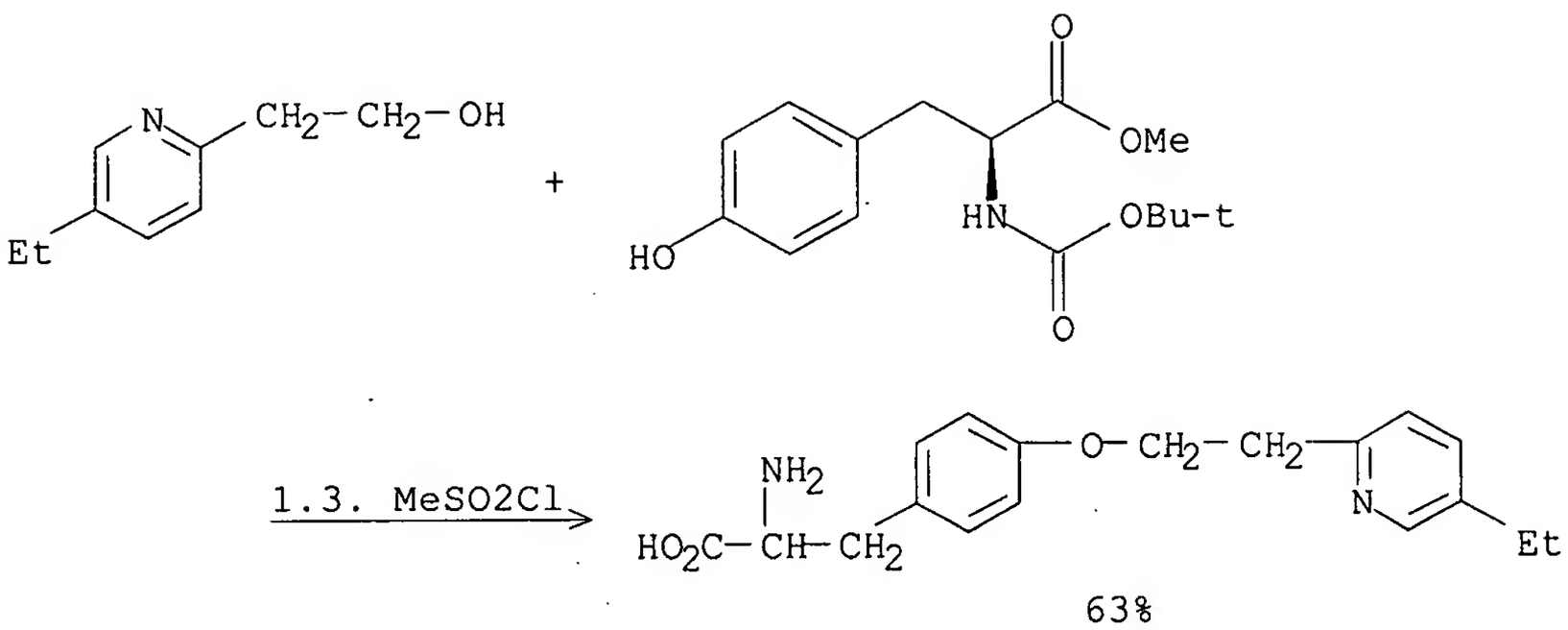


63%

NOTE: 3) last stage neutralization

Updated Search

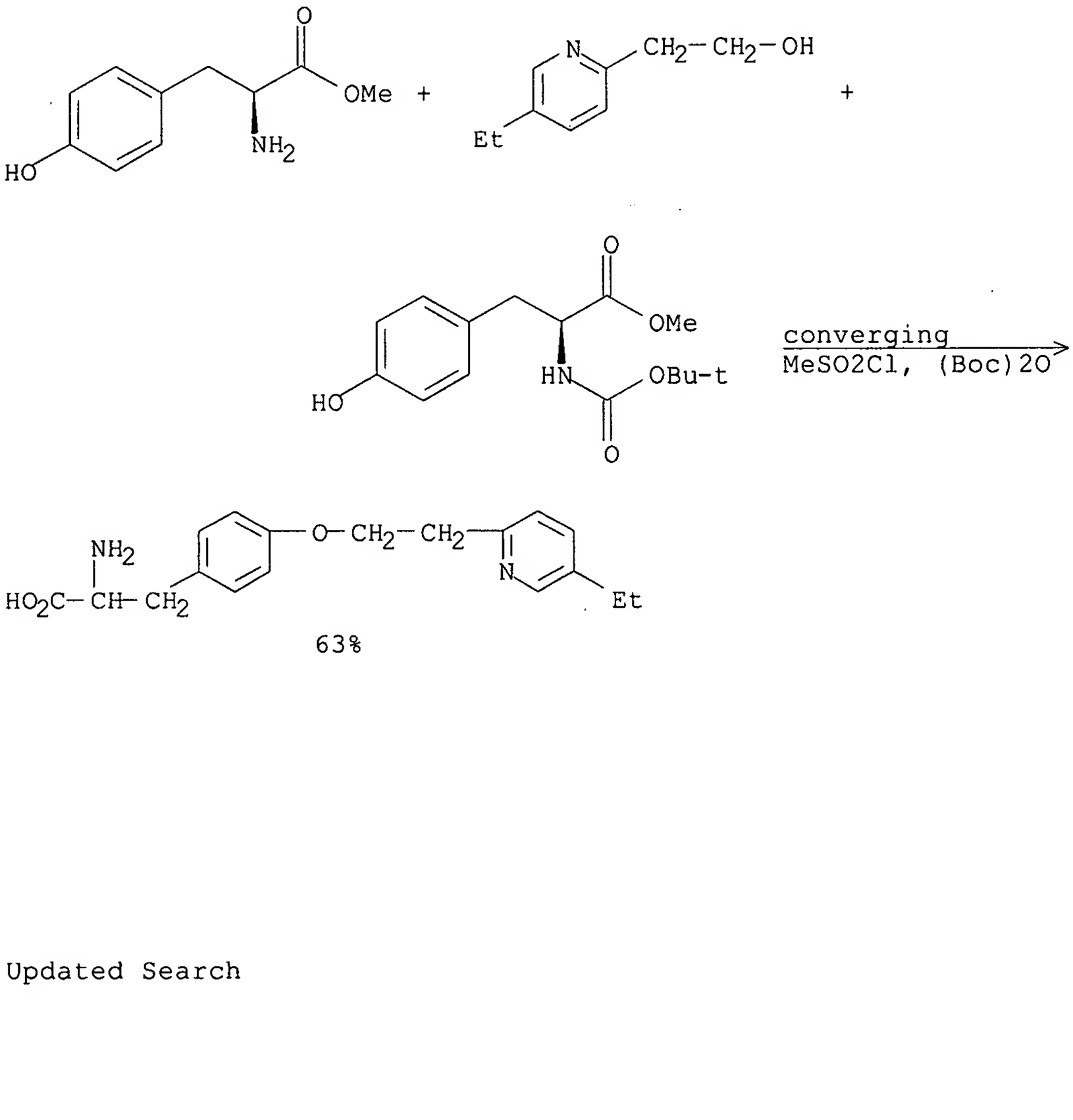
RX(54) OF 80 - 4 STEPS



63%

NOTE: 4) last stage neutralization
CON: STEP(1.1) room temperature
STEP(1.2) room temperature -> 0 deg C
STEP(1.3) 75 minutes, 0 - 10 deg C; 10 deg C -> room temperature;
1 hour, room temperature

RX(70) OF 80 - 5 STEPS

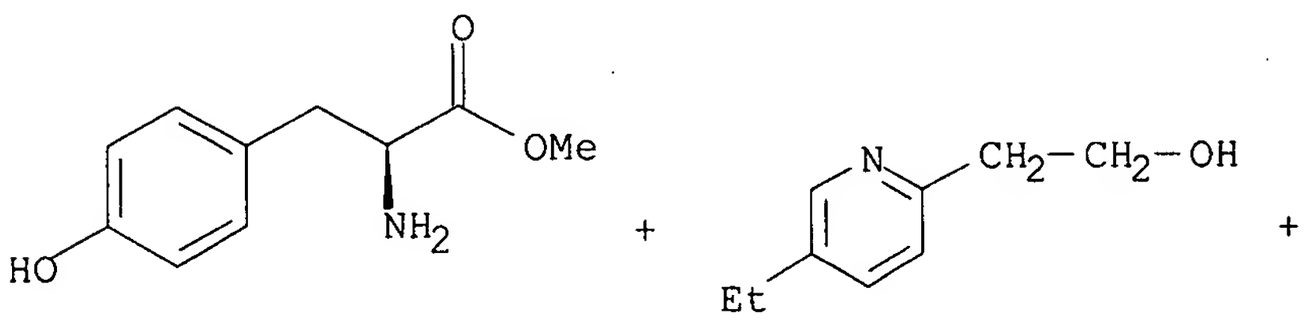


63%

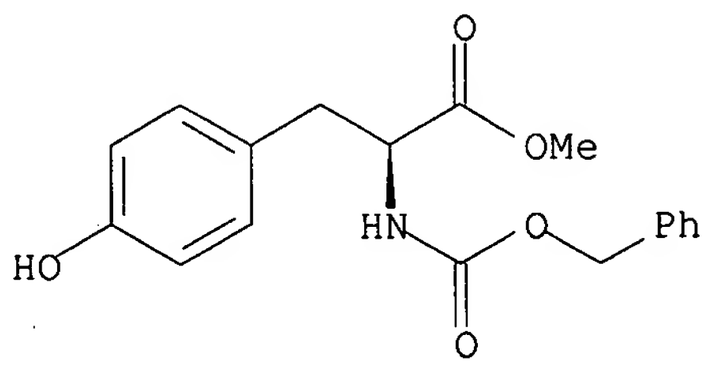
Updated Search

NOTE: last stage neutralization, last stage quench
CON: STEP(1.1) room temperature
STEP(1.2) room temperature -> 0 deg C
STEP(1.3) 75 minutes, 0 - 10 deg C; 10 deg C -> room temperature;
1 hour, room temperature

RX(72) OF 80 - 4 STEPS

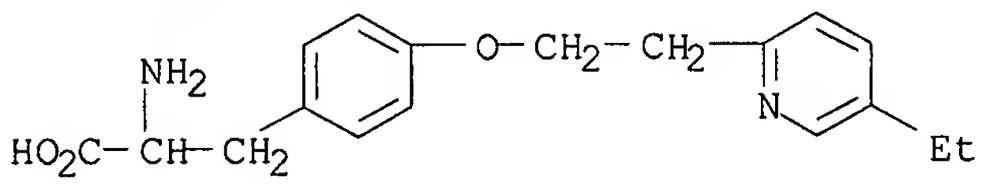


HCl



converging
MeSO2Cl
ClCO2CH2Ph

RX(72) OF 80 - 4 STEPS



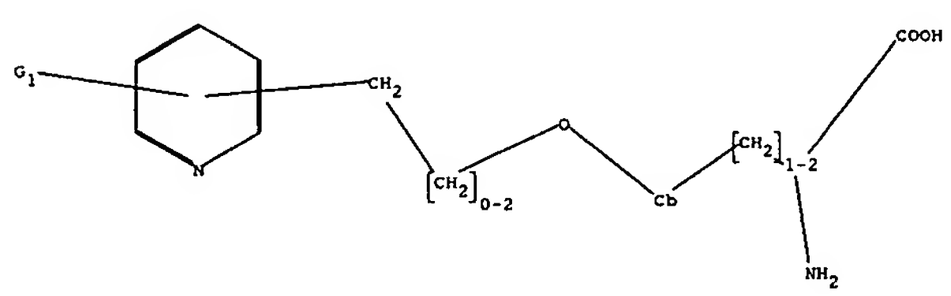
22%

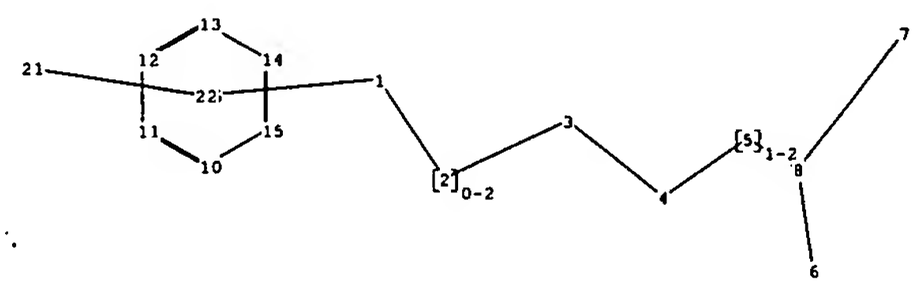
NOTE: last stage neutralization
CON: STEP(1.1) room temperature
STEP(1.2) room temperature -> 0 deg C
STEP(1.3) 75 minutes, 0 - 10 deg C; 10 deg C -> room temperature;
1 hour, room temperature

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Updated Search

C:\Documents and Settings\brobinson1\My Documents\stnweb\Queries\45454lpi.str





chain nodes :
1 2 3 4 5 6 7 8 21
ring nodes :
10 11 12 13 14 15
chain bonds :
1-2 2-3 3-4 4-5 5-8 6-8 7-8
ring bonds :
10-11 10-15 11-12 12-13 13-14 14-15
exact/norm bonds :
6-8
exact bonds :
1-2 2-3 3-4 4-5 5-8 7-8
normalized bonds :
10-11 10-15 11-12 12-13 13-14 14-15
isolated ring systems :
containing 10 :

G1:CH3,Et

Match level :
1:CLASS 2:CLASS 3:CLASS 4:Atom 5:CLASS 6:CLASS 7:CLASS 8:CLASS
10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS 21:CLASS
22:Atom
Generic attributes :
4:
Saturation : Unsaturated
Number of Carbon Atoms : less than 7
Type of Ring System : Polycyclic

Element Count :
Node 4: Limited
C,C6

10555659

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1612bxr

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'CAOLD' AT 20:13:56 ON 02 APR 2007
FILE 'CAOLD' ENTERED AT 20:13:56 ON 02 APR 2007
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.45	1424.50

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-1.56

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.45	1424.50

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-1.56

FILE 'REGISTRY' ENTERED AT 20:14:05 ON 02 APR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 1 APR 2007 HIGHEST RN 928822-97-3
DICTIONARY FILE UPDATES: 1 APR 2007 HIGHEST RN 928822-97-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Documents and Settings\brobinson1\My
Documents\stnweb\Queries\1212lkj.str

Updated Search

10555659

L41 STRUCTURE UPLOADED

=> s l41
SAMPLE SEARCH INITIATED 20:17:53 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 62928 TO ITERATE

3.2% PROCESSED 2000 ITERATIONS 0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **INCOMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1243614 TO 1273506
PROJECTED ANSWERS: 0 TO 0

L42 0 SEA SSS SAM L41

=>
Uploading C:\Documents and Settings\brobinson1\My Documents\stnweb\Queries\2323k.str

L43 STRUCTURE UPLOADED

=> s l43
SAMPLE SEARCH INITIATED 20:19:30 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 62805 TO ITERATE

3.2% PROCESSED 2000 ITERATIONS 0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **INCOMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1241169 TO 1271031
PROJECTED ANSWERS: 0 TO 0

L44 0 SEA SSS SAM L43

=>
Uploading C:\Documents and Settings\brobinson1\My
Documents\stnweb\Queries\45454lpi.str

L45 STRUCTURE UPLOADED

=> s l45
SAMPLE SEARCH INITIATED 20:23:26 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 2951 TO ITERATE

67.8% PROCESSED 2000 ITERATIONS 0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 55762 TO 62278
PROJECTED ANSWERS: 0 TO 0

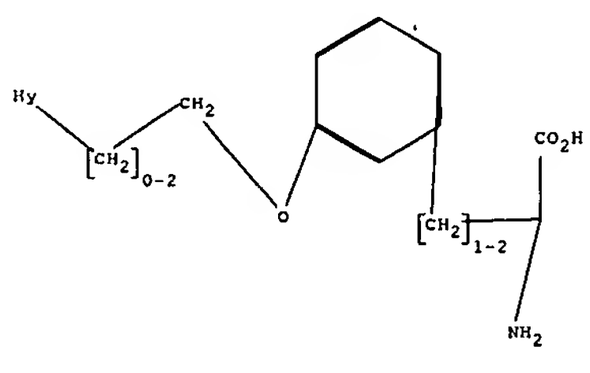
L46 0 SEA SSS SAM L45

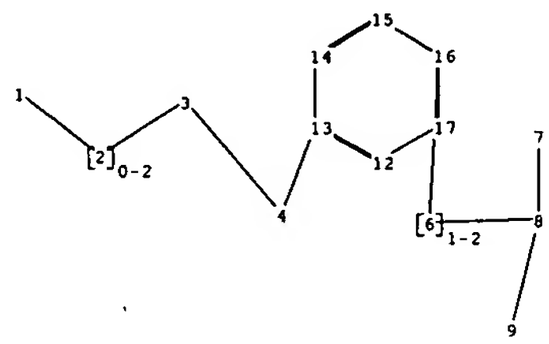
Updated Search

```
10555659

=> s l45 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 171.65 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 20:23:30 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    58334 TO ITERATE

100.0% PROCESSED    58334 ITERATIONS                                  0 ANSWERS
SEARCH TIME: 00.00.01

L47             0 SEA SSS FUL L45
```

Updated Search

C:\Documents and Settings\brobinson1\My Documents\stnweb\Queries\34ae34.str





chain nodes :
1 2 3 4 6 7 8 9
ring nodes :
12 13 14 15 16 17
chain bonds :
1-2 2-3 3-4 4-13 6-8 6-16 7-8 8-9
ring bonds :
12-13 12-17 13-14 14-15 15-16 16-17
exact/norm bonds :
1-2 4-13 8-9
exact bonds :
2-3 3-4 6-8 6-16 7-8
normalized bonds :
12-13 12-17 13-14 14-15 15-16 16-17

Match level :
1:Atom 2:CLASS 3:CLASS 4:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS
12:Atom 13:Atom 14:CLASS 15:CLASS 16:Atom 17:Atom
Generic attributes :
1:
Saturation : Unsaturated
Number of Carbon Atoms : less than 7
Number of Hetero Atoms : Exactly 1
Type of Ring System : Monocyclic

Element Count :
Node 1: Limited
C,C5
N,N1

10555659

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1612bxr

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 4	DEC 18	CA/CAplus patent kind codes updated
NEWS 5	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS 6	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS 7	DEC 27	CA/CAplus enhanced with more pre-1907 records
NEWS 8	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 9	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 10	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 11	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 12	JAN 22	CA/CAplus updated with revised CAS roles
NEWS 13	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS 14	JAN 29	PHAR reloaded with new search and display fields
NEWS 15	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 16	FEB 15	PATDPASPC enhanced with Drug Approval numbers
NEWS 17	FEB 15	RUSSIAPAT enhanced with pre-1994 records
NEWS 18	FEB 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS 19	FEB 26	MEDLINE reloaded with enhancements
NEWS 20	FEB 26	EMBASE enhanced with Clinical Trial Number field
NEWS 21	FEB 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS 22	FEB 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 23	FEB 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
NEWS 24	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS 25	MAR 16	CASREACT coverage extended
NEWS 26	MAR 20	MARPAT now updated daily
NEWS 27	MAR 22	LWPI reloaded
NEWS 28	MAR 30	RDISCLOSURE reloaded with enhancements
NEWS 29	MAR 30	INPADOCDB will replace INPADOC on STN
NEWS 30	APR 02	JICST-EPLUS removed from database clusters and STN

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

Updated Search

10555659

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:09:18 ON 09 APR 2007

=> file reg
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.42	0.42

FILE 'REGISTRY' ENTERED AT 11:10:08 ON 09 APR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 8 APR 2007 HIGHEST RN 929518-97-8
DICTIONARY FILE UPDATES: 8 APR 2007 HIGHEST RN 929518-97-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Documents and Settings\brobinson1\My Documents\stnweb\Queries\565659o1.str

L1 STRUCTURE UPLOADED

=> s l1 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 171.65 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 11:15:04 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 1254466 TO ITERATE

64.9% PROCESSED 813553 ITERATIONS 9 ANSWERS

79.7% PROCESSED 1000000 ITERATIONS 13 ANSWERS

Updated Search

```
10555659

INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.31

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:      1254466 TO  1254466
PROJECTED ANSWERS:              13 TO       28

L2            13 SEA SSS FUL L1

=>
Uploading C:\Documents and Settings\brobinson1\My
Documents\stnweb\Queries\34ae34.str

L3      STRUCTURE UPLOADED

=> s l3
SAMPLE SEARCH INITIATED 11:16:43 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     1708 TO ITERATE

100.0% PROCESSED     1708 ITERATIONS                                 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        31681 TO    36639
PROJECTED ANSWERS:               0 TO        0

L4             0 SEA SSS SAM L3

=> s l3 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 171.65 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 11:16:48 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    34029 TO ITERATE

100.0% PROCESSED    34029 ITERATIONS                               14 ANSWERS
SEARCH TIME: 00.00.01

L5            14 SEA SSS FUL L3

=> file hcaplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                               ENTRY     SESSION
FULL ESTIMATED COST                           348.25      348.67

FILE 'HCAPLUS' ENTERED AT 11:16:52 ON 09 APR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
the American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing


Updated Search
```

FILE COVERS 1907 - 9 Apr 2007 VOL 146 ISS 16
FILE LAST UPDATED: 8 Apr 2007 (20070408/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

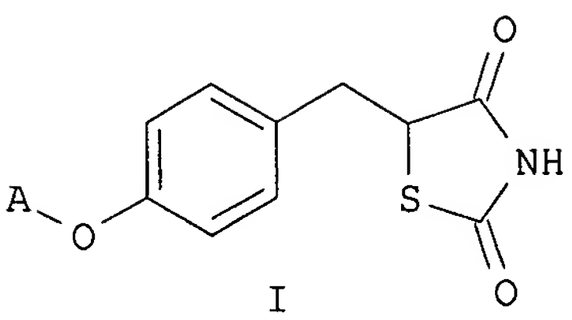
This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s l5
L6             7 L5

=> s l6 and duran, e?/au
            115 DURAN, E?/AU
L7            0 L6 AND DURAN, E?/AU
```

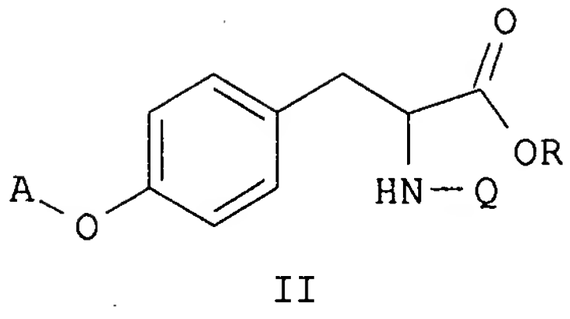
```
=> d l6, ibib abs hitstr, 1-7

L6   ANSWER 1 OF 7  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2004:1016040  HCAPLUS
DOCUMENT NUMBER:          141:424180
TITLE:                    Processes for making thiazolidinedione derivatives and
                          compounds thereof
INVENTOR(S):              Pospisilik, Karel; Zhu, Jie; Picha, Frantisek
PATENT ASSIGNEE(S):       Synthon B.V., Neth.
SOURCE:                   PCT Int. Appl., 47 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.            KIND   DATE        APPLICATION NO.          DATE
     ----------------      ----   --------    --------------------     --------
     WO 2004101560          A1    20041125    WO 2004-EP5026           20040511
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW:  BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
     US 2005059708          A1    20050317    US 2004-842635           20040511
     EP 1622898             A1    20060208    EP 2004-732115           20040511
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
     CN 1812988             A     20060802    CN 2004-80018359         20040511
     JP 2007502847          T     20070215    JP 2006-529780           20040511
PRIORITY APPLN. INFO.:                       US 2003-469837P      P   20030513
                                             WO 2004-EP5026       W   20040511

OTHER SOURCE(S):          MARPAT 141:424180
GI
```

Updated Search

10555659



I



II

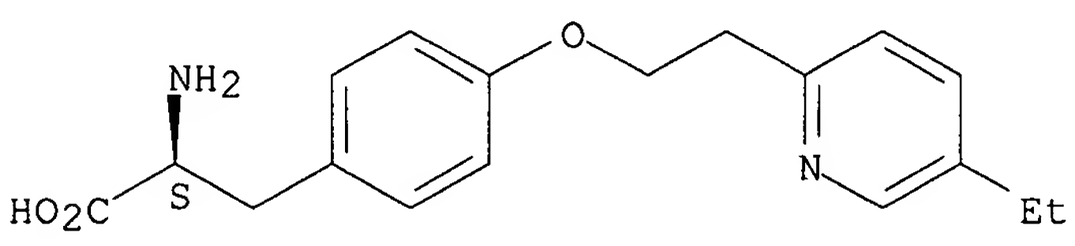
AB The invention relates processes for the synthesis of thiazolidinedione derivs. I (A is ethyl-2-pyridylethyl, [(2-pyridyl)methylamino]ethyl or [3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methyl] via reactions of amino acid intermediates II (same A, R is H or alkyl, Q is H or an amine-protecting group). The synthesis of pioglitazone is illustrated. Thus, 2-amino-3-[4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl]propionic acid, prepared by O-alkylation of L-tyrosine, underwent diazotization reaction to give the 2-bromo derivative which underwent cyclocondensation with thiourea to afford pioglitazone (isolated as the HCl salt).

IT 794591-56-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(Processes for making thiazolidinedione derivs. and compds. thereof)

RN 794591-56-3 HCAPLUS

CN L-Tyrosine, O-[2-(5-ethyl-2-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:996131 HCAPLUS

DOCUMENT NUMBER: 141:424428

TITLE: Intermediate compound, namely O-[2-(5-ethylpyridin-2-yl)ethyl]tyrosine, which is used for the preparation of the antidiabetic agent pioglitazone, and methods for its preparation and conversion to pioglitazone

INVENTOR(S): Duran, Lopez Ernesto

PATENT ASSIGNEE(S): Medichem, S.A., Spain

SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Spanish

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004099147	A1	20041118	WO 2004-ES70031	20040504

Updated Search

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

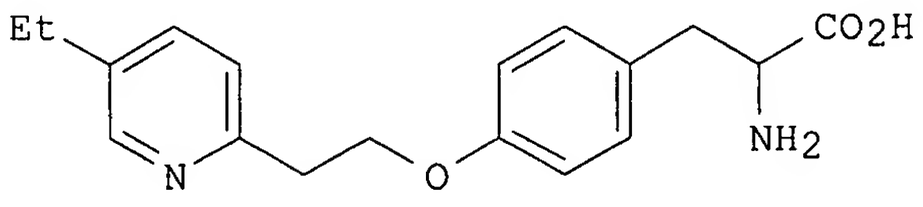
ES 2219180	A1	20041116	ES 2003-1075	20030509
ES 2219180	B1	20060301		
CA 2525190	A1	20041118	CA 2004-2525190	20040504
EP 1623977	A1	20060208	EP 2004-731028	20040504

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

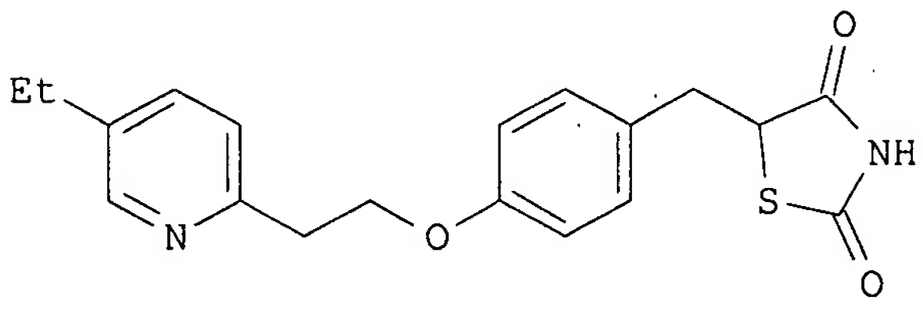
PRIORITY APPLN. INFO.: ES 2003-1075 A 20030509
WO 2004-ES70031 W 20040504

OTHER SOURCE(S): CASREACT 141:424428; MARPAT 141:424428

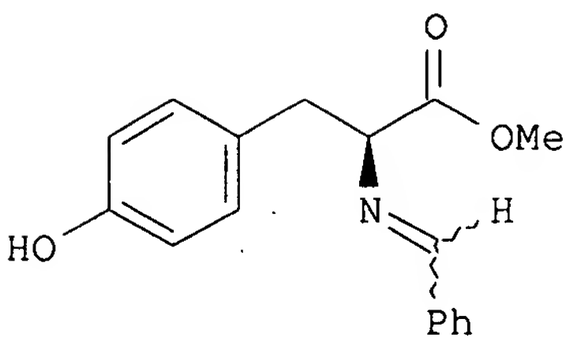
GI



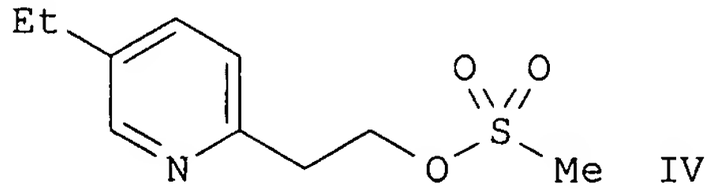
I



II



III



IV

AB The invention relates to the novel O-substituted tyrosine derivative I, including pure or mixed enantiomers, racemates, salts, solvates, and hydrates. I and its stereoisomers and compds. are new key intermediates for the preparation of the antidiabetic agent pioglitazone (II). The invention also relates to a method of obtaining I from a natural product, L-tyrosine, in which the amino group, in the form of an aromatic imine group,

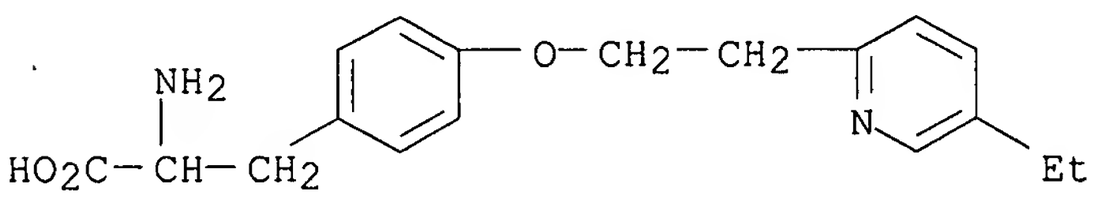
Updated Search

is protected by an aldehyde or ketone. The invention further relates to a method of obtaining II from the intermediate compound I. The critical feature of the invention is protection of the tyrosine N-terminal as an imine, which allows etherification of the phenolic tyrosine OH group to occur without competing N-alkylation. Complete racemization during the process allows the more desirable racemic I to be prepared from the more readily available L-tyrosine. For instance, L-tyrosine was treated with SOCl2 in refluxing MeOH to give the Me ester, which was treated with PhCHO at room temperature in CH2Cl2 to give doubly protected tyrosine III. This phenolic compound was etherified with the mesylate IV (preparation given) using K2CO3 and Bu4N+Br- in PhMe at 70°, and the protected product was deprotected in situ first with acid (2N HCl) and then with base (50% NaOH), both at 70°, to give racemic I in 62.8% overall yield from L-tyrosine. Diazotization of the amino group in I in the presence of HBr gave the corresponding bromo compound, which was cyclized with thiourea to give the 2-imine derivative of II. Acid hydrolysis of the imine in refluxing aqueous HCl gave II in 40.7% yield from I. Four comparative processes for preparing I, using other standard amine protecting groups instead of a benzaldehyde imine, were examined Overall yields of I from L-tyrosine were 24.1% for Boc, 20.7% for Cbz, 11.5% for Ac, and poor (unisolated) for EtOCO, vs. 62.8% for benzylidene.

IT 795316-22-2P, O-[2-(5-Ethylpyridin-2-yl)ethyl]-DL-tyrosine
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(target intermediate; intermediate compound which is used for the preparation of pioglitazone)

RN 795316-22-2 HCAPLUS

CN Tyrosine, O-[2-(5-ethyl-2-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)

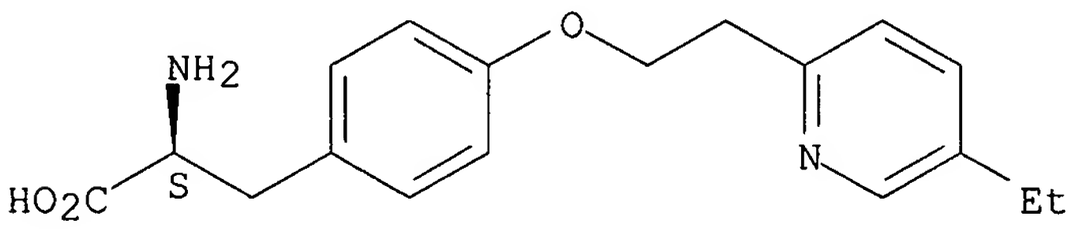


IT 794591-56-3P, O-[2-(5-Ethylpyridin-2-yl)ethyl]-L-tyrosine
795316-27-7P, O-[2-(5-Ethylpyridin-2-yl)ethyl]-D-tyrosine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(target intermediate; intermediate compound which is used for the preparation of pioglitazone)

RN 794591-56-3 HCAPLUS

CN L-Tyrosine, O-[2-(5-ethyl-2-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



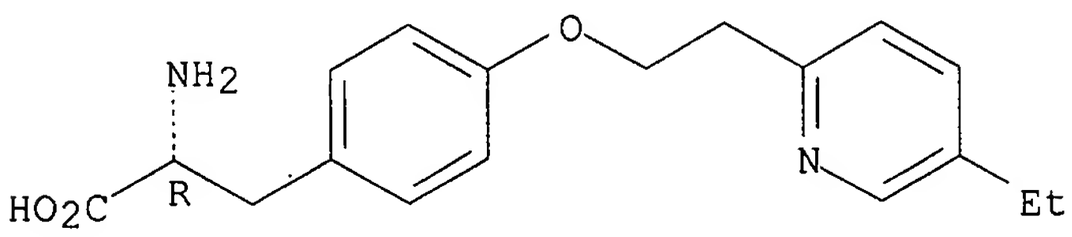
RN 795316-27-7 HCAPLUS

Updated Search

10555659

CN D-Tyrosine, O-[2-(5-ethyl-2-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

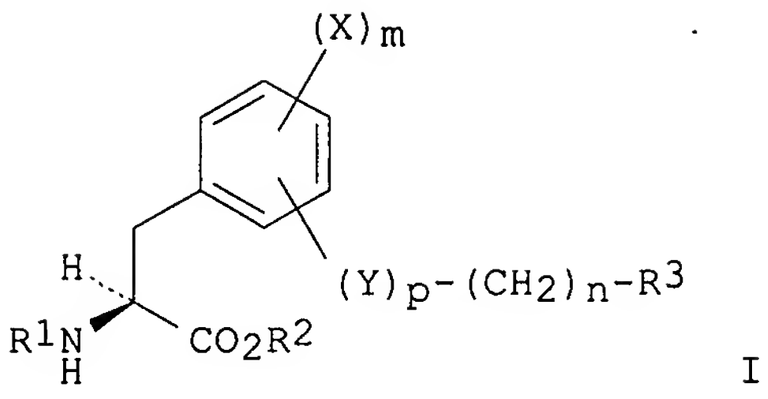
L6 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:633643 HCAPLUS
DOCUMENT NUMBER: 139:180343
TITLE: Preparation of aromatic amino acid derivatives as anticancer agents
INVENTOR(S): Endo, Hitoshi; Kanai, Yoshikatsu; Tsujihara, Kenji; Saito, Kunio
PATENT ASSIGNEE(S): Japan
SOURCE: PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003066574	A1	20030814	WO 2003-JP1081	20030203
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2475434	A1	20030814	CA 2003-2475434	20030203
AU 2003208105	A1	20030902	AU 2003-208105	20030203
EP 1481965	A1	20041201	EP 2003-703151	20030203
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005119256	A1	20050602	US 2003-503125	20030203
CN 1630632	A	20050622	CN 2003-803549	20030203
PRIORITY APPLN. INFO.:			JP 2002-31216 A	20020207
			WO 2003-JP1081 W	20030203

OTHER SOURCE(S): MARPAT 139:180343
GI

Updated Search

10555659



I

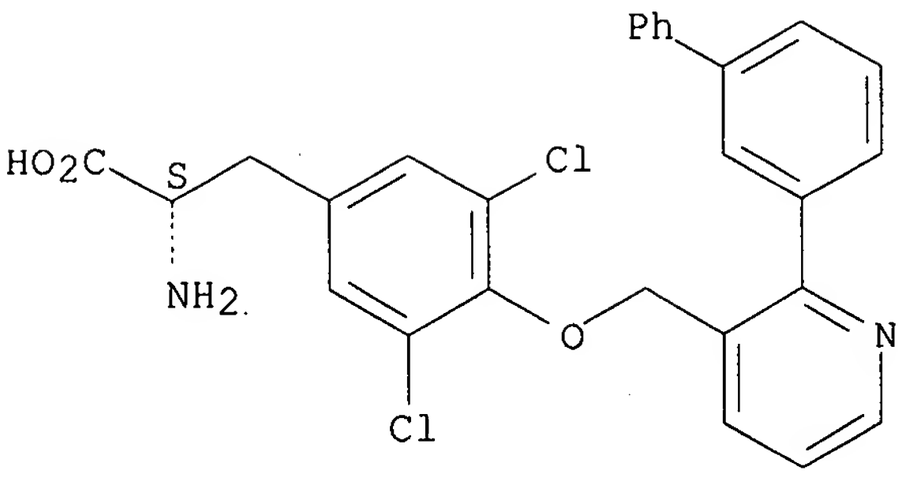
AB Aromatic amino acid derivs. represented by the following general formula (I) or pharmacol. acceptable salts thereof [wherein R1 represents hydrogen or an amino-protecting group; R2 represents hydrogen, alkylaralkyl or aryl; R3 represents (1) halogeno, (2) aroylamino, (3) Ph substituted by lower alkyl, Ph, phenoxy, etc., (4) naphthyl or tetrahydronaphthyl optionally substituted by hydroxy, lower alkoxy or di(lower alkyl)amino, (5) an N-, O- and/or S-containing unsatd. monocyclic heterocycle group substituted by lower alkyl, Ph, naphthyl or tetrahydroquinolyl, or (6) an N-, O- and/or S-containing fused heterocycle group, which may be unsatd. or partly saturated, optionally substituted by oxo, carboxy, amino, lower alkyl, etc.; X represents halogeno, alkyl or alkoxy; Y represents oxygen or nitrogen; p is 0 or 1; m is 0, 1 or 2; and n is an integer of from 0 to 5] are prepared These compds. inhibit a transporter (LAT1) of essential amino acids which are one of the main nutrients for cancer cells and induce depletion of the essential amino acids in the cancer cells, thereby inhibit the proliferation of the cancer cells. Thus, 0.2 mL pyridine was added to a suspension of N-trifluoroacetyl-3-hydroxy-L-phenylalanine Et ester 159, 2-naphthaleneboronic acid 186, mol. sieve 4A 204, and Cu(OAc)2 153 mg in 7 mL CH2Cl2, stirred at room temperature for 16 h in air to give, after workup and silica gel chromatog., 89% N-trifluoroacetyl-3-(2-naphthyloxy)-L-phenylalanine Et ester (II). 0.5 N aqueous NaOH was added to a solution of II (94 mg) in 2 mL THF at 5°, stirred at 5° for 69 h, acidified with 1 N aqueous HCl to pH 3-4, and filtered to give 78% 3-(2-naphthyloxy)-L-phenylalanine (III). In an assay for a LAT1 inhibitory activity, III and 3-[3-(6-dimethylaminopyridyl)phenoxy]-L-phenylalanine in vitro showed IC50 of 0.1 and 0.01 μg/mL, resp., for inhibiting the uptake of [14C]-L-tyrosine by human prostatic cancer T24 cells.

IT 579524-57-5P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of aromatic amino acid derivs. as anticancer agents for inhibiting proliferation of cancer cells by inhibiting essential amino acid transporter (LAT1))

RN 579524-57-5 HCAPLUS
CN L-Tyrosine, O-[(2-[1,1'-biphenyl]-3-yl-3-pyridinyl)methyl]-3,5-dichloro- (9CI) (CA INDEX NAME)

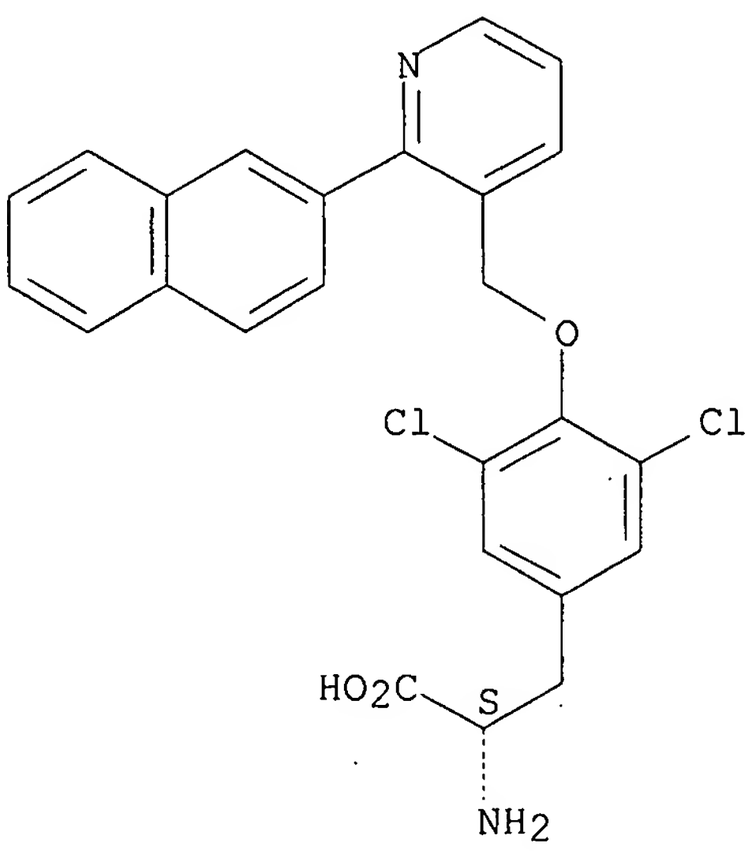
Absolute stereochemistry.

Updated Search



IT 579524-58-6P 579524-59-7P 579524-66-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aromatic amino acid derivs. as anticancer agents for inhibiting
proliferation of cancer cells by inhibiting essential amino acid transporter (LAT1))
RN 579524-58-6 HCAPLUS
CN L-Tyrosine, 3,5-dichloro-O-[[2-(2-naphthalenyl)-3-pyridinyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

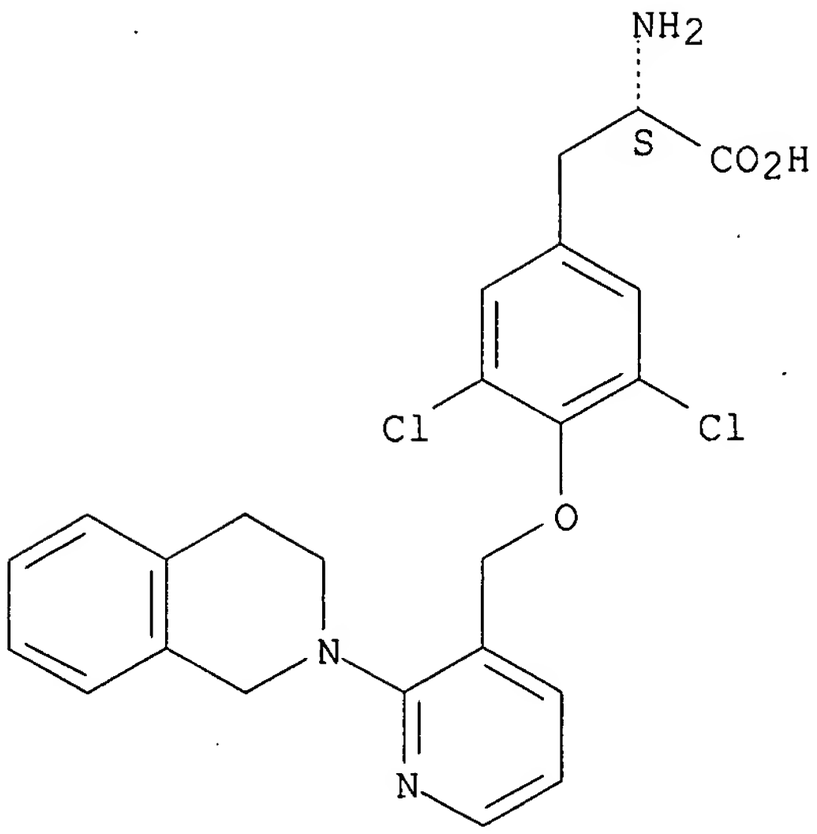


RN 579524-59-7 HCAPLUS
CN L-Tyrosine, 3,5-dichloro-O-[[2-(3,4-dihydro-2(1H)-isoquinolinyl)-3-pyridinyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

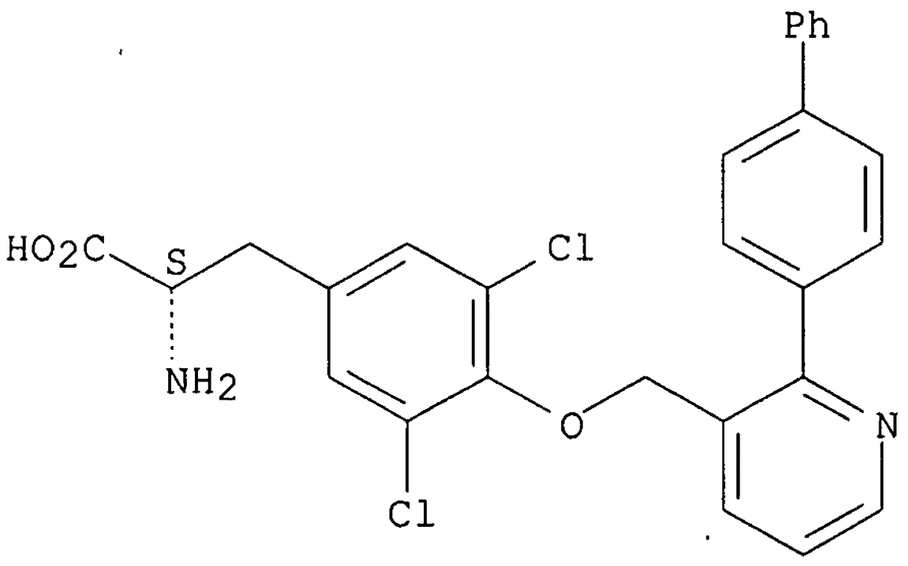
Updated Search

10555659



RN 579524-66-6 HCAPLUS
CN L-Tyrosine, O-[(2-[1,1'-biphenyl]-4-yl-3-pyridinyl)methyl]-3,5-dichloro-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:888693 HCAPLUS
DOCUMENT NUMBER: 137:385108
TITLE: Preparation of 2-amino-3-[3,5-dibromo-4-(3-bromobenzyloxy)phenyl]propionic acid and related compounds as thyroid hormone receptor antagonists for cardiac and metabolic disorders
INVENTOR(S): Malm, Johan; Brandt, Peter; Edvinsson, Karin; Ericsson, Thomas; Gordon, Sandra
PATENT ASSIGNEE(S): Karo Bio AB, Swed.
SOURCE: PCT Int. Appl., 40 pp..
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

Updated Search

10555659

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002092550	A1	20021121	WO 2002-EP4193	20020415
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2446747	A1	20021121	CA 2002-2446747	20020415
EP 1387825	A1	20040211	EP 2002-735262	20020415
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1509267	A	20040630	CN 2002-809941	20020415
JP 2004533450	T	20041104	JP 2002-589436	20020415
US 2004220147	A1	20041104	US 2004-477676	20040610
PRIORITY APPLN. INFO.:			GB 2001-11861 A	20010515
			WO 2002-EP4193 W	20020415

OTHER SOURCE(S): MARPAT 137:385108

AB Compds. 3,5,4-R2,R3(R1CH2O)C6H2(CH2)nCHR4R5 [I; R1 = (un)substituted (hetero)aryl or cycloalkyl; R2, R3 = Cl, Br, (cyclo)alkyl, alkenyl, alkynyl; R4 = halo, OH, SH, NH2, alkylamino; R5 = CO2H, PO3H2, P(O)(OH)NH2, SO3H, COCO2H, CONHOH; n = 1 or 2], including all possible stereoisomers, prodrug esters, and radioactive forms, were prepared as thyroid receptor ligands, preferably antagonists, for the treatment of cardiac arrhythmias, thyrotoxicosis, subclin. hyperthyroidism, and liver diseases. Thus, the title acid was prepared from Boc-Tyr-OMe (Boc = tert-butoxycarbonyl) by bromination, etherification with 3-bromobenzyl bromide, and deprotection using TFA. I exhibited binding affinities to the thyroid hormone receptor α (ThRa) in the range of 100 nM to 10,000 nM. Compds. I exhibited binding affinities to the ThRa receptor in the range of 10 nM to 10,000 nM.

IT 475999-13-4P 475999-31-6P
RL: DGN (Diagnostic use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino[(benzyloxy)phenyl]propionic acid derivs. and related compds. as thyroid hormone receptor antagonists for cardiac and metabolic disorders)

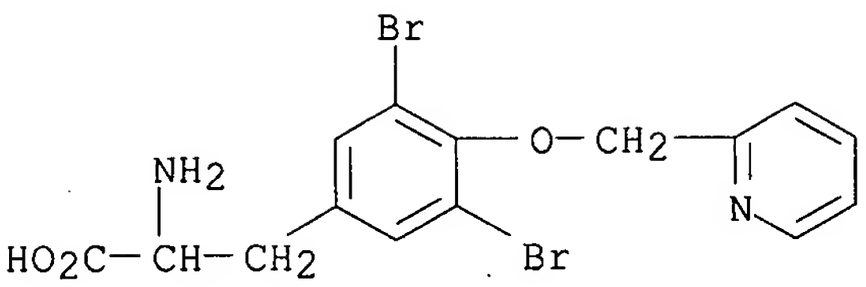
RN 475999-13-4 HCAPLUS
CN Tyrosine, 3,5-dibromo-O-(2-pyridinylmethyl)-, compd. with N,N-diethylethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 475999-12-3
CMF C15 H14 Br2 N2 O3

Updated Search

10555659



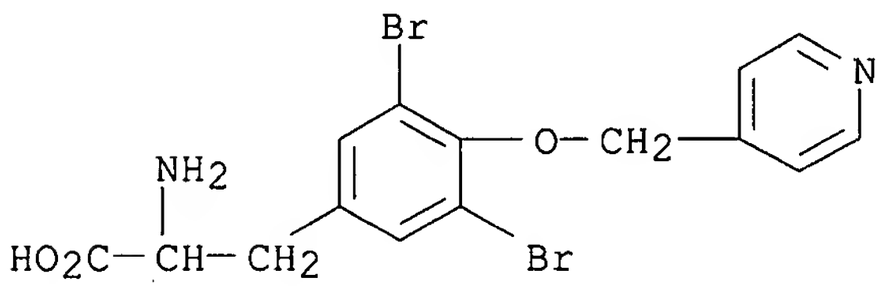
CM 2

CRN 121-44-8
CMF C6 H15 N

RN 475999-31-6 HCAPLUS
CN Tyrosine, 3,5-dibromo-O-(4-pyridinylmethyl)-, compd. with N,N-diethylethanamine (1:1) (9CI) (CA INDEX NAME)

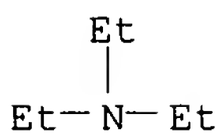
CM 1

CRN 475999-30-5
CMF C15 H14 Br2 N2 O3



CM 2

CRN 121-44-8
CMF C6 H15 N



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:863150 HCAPLUS
DOCUMENT NUMBER: 134:157200
TITLE: Development of potent and selective plasmin and plasma kallikrein inhibitors and studies on the structure-activity relationship

Updated Search

10555659

AUTHOR(S): Okada, Yoshio; Tsuda, Yuko; Tada, Mayako; Wanaka, Keiko; Okamoto, Utako; Hijikata-Okunomiya, Akiko; Okamoto, Shosuke
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, and High Technology Research Center, Kobe Gakuin University, Kobe, 651-2180, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (2000), 48(12), 1964-1972
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Based on structure-activity relationship studies, we designed and synthesized plasmin (PL) and plasma kallikrein (PK) inhibitors. Trans-(4-aminomethylcyclohexanecarbonyl)-Tyr(O-Pic)-octylamide inhibited PL, PK, urokinase (UK) and thrombin (TH) with IC50 values of 0.53, 30, 5.3 and >400 μM, resp. Trans-(4-aminomethylcyclohexanecarbonyl)-Tyr(O-2-Pyrim)-4-carboxyanilide inhibited PL, PK, UK and TH with IC50 values of 36, 0.56, 440 and >1000 μM, resp.

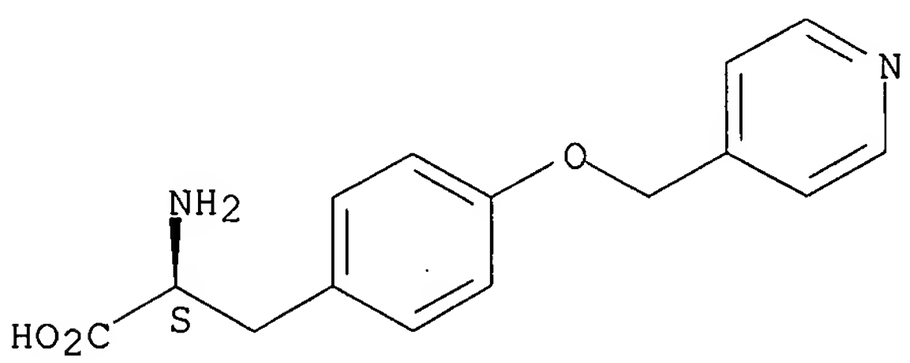
IT 325464-36-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(plasmin and plasma kallikrein inhibitors: structure-activity relationship)

RN 325464-36-6 HCAPLUS
CN L-Tyrosine, O-(4-pyridinylmethyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

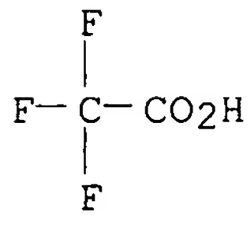
CRN 39837-02-0
CMF C15 H16 N2 O3

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS

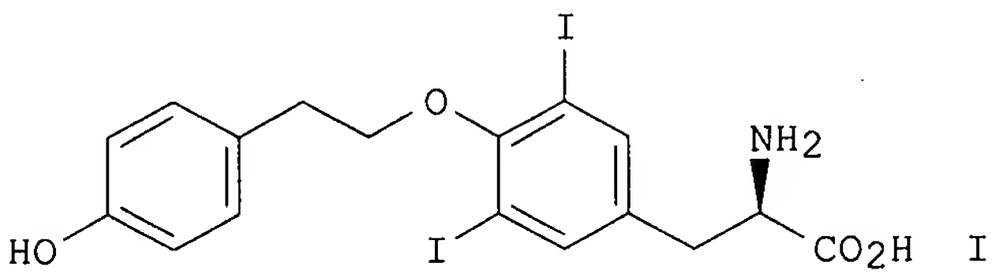
Updated Search

10555659

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:344485 HCAPLUS
DOCUMENT NUMBER: 125:87188
TITLE: Synthesis and SAR of diiodotyrosine-derived glycine-site N-methyl-D-aspartate receptor ligands
AUTHOR(S): Curtis, Neil R.; Kulagowski, Janusz J.; Leeson, Paul D.; Mawer, Ian M.; Ridgill, Mark P.; Rowley, Michael; Grimwood, Sarah; Marshall, George R.
CORPORATE SOURCE: Merck Sharp & Res. Lab., Neurosci. Res. Centre, Harlow, CM20 2QK, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (1996), 6(10), 1145-1150
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

GI

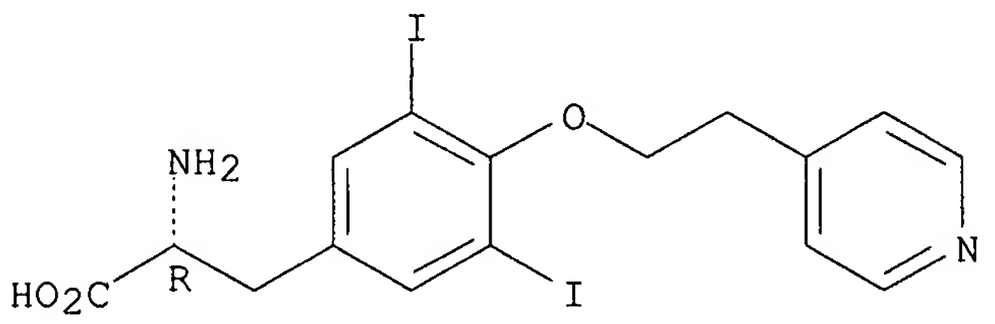


AB A series of analogs of the novel diiodotyrosine derived N-methyl-D-aspartate (NMDA) glycine-site ligand (R)-I was prepared in which the aryl substitution, chain length and amino acid groups were varied. The key structural features for binding are the α-amino acid function, having the (R)-absolute stereochem., the 3,5-diiodo substituted aromatic ring and a lipophilic group attached at the tyrosine phenolic oxygen.

IT 178666-05-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and structure-activity of diiodotyrosine-derived glycine-site methylaspartate receptor ligands)

RN 178666-05-2 HCAPLUS
CN D-Tyrosine, 3,5-diiodo-O-[2-(4-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2007 ACS on STN

Updated Search

10555659

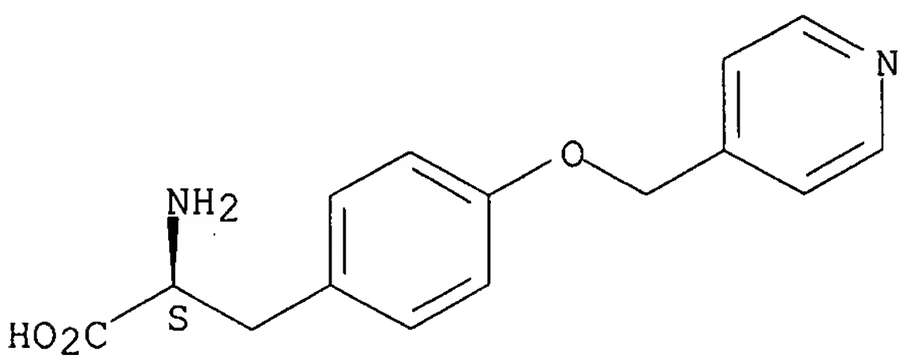
ACCESSION NUMBER: 1973:4506 HCAPLUS
DOCUMENT NUMBER: 78:4506
TITLE: Protection of thiol and phenolic hydroxy-groups as their 4-picolyl ethers, cleaved by electrolytic reduction
AUTHOR(S): Gosden, A.; Stevenson, D.; Young, G. T.
CORPORATE SOURCE: Dyson Perrins Lab., Oxf. Univ., Oxford, UK
SOURCE: Journal of the Chemical Society, Chemical Communications (1972), (20), 1123-4
CODEN: JCCCAT; ISSN: 0022-4936
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The 4-picolyl group (Pic), removable by electrolytic reduction, was used to protect the thiol group of cysteine and the hydroxy group of tyrosine during peptide synthesis. Thus, reduction of L-cysteine with Na in liquid NH3 followed by treatment with PicCl gave 68% Pic-Cys which with BocN3 (Boc = Me3COCO) gave 87% Boc-Cys-Pic (I). Gly-OEt with I and dicyclohexylcarbodiimide followed by hydrolysis with aqueous NaOH gave Boc-Cys(Pic)-Gly which on electrolytic reduction followed by air oxidation gave 75% Gly-Cys-Cys-Gly. Similarly Pic-Tyr was used in the preparation of Tyr-Gly.

IT 39837-02-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 39837-02-0 HCAPLUS
CN L-Tyrosine, O-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> file caold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	47.29	395.96

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-5.46	-5.46

FILE 'CAOLD' ENTERED AT 11:19:28 ON 09 APR 2007

FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent

Updated Search